Methods: The surveyed centers accounted for 75% of all pediatric HSCT and were identified by querying the CIBMTR. Two individuals from each of these institutions were survey recipients; one from the Division of Pediatric Critical Care Medicine (PCCM) and the other from the Division of HSCT. The survey was conducted electronically using SurveyMonkey allowing data to remain anonymous. A four-choice Lickert scale was used for clinical questions.

Results: Completed surveys were returned from both the HSCT and PCCM physicians in 22 programs. The percentage of programs that always or commonly perform the following interventions on the HSCT unit are as follows: central venous pressure monitoring (18%), 100% non-rebreather mask (50%), non-invasive ventilation(18%), intermittent hemodialysis (41%), continuous veno-venous hemofiltration (0%), dopamine (36%) with the maximal dose varying by center. In terms of care by PCCM physicians, most all programs use 100% oxygen, non-invasive ventilation and aggressive diuresis prior to intubation; 2/3 of programs attempt renal replacement therapy (RRT). 59% of PCCM physicians always or commonly offer intubation as a time limited trial to HSCT patients; 18% never offer this option. Non-conventional respiratory therapies commonly offered to HSCT patients include high frequency oscillatory ventilation, nitric oxide and RRT. Surfactant use is less common and ECMO use is rare.

Conclusion: There is a notable variation in the level of monitoring and support offered on pediatric HSCT units as well as therapies provided by PCCM physicians to HSCT patients. Not only is this data is important for the design of clinical trials, but studies should be done to determine if these practice variations impact patient outcomes.

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SURVIVAL FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION FOR CONGENITAL IMMUNODEFICIENCY AND METABOLIC DISORDERS

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We compared outcomes of allogeneic stem cell transplantation (SCT) for congenital immunodeficiency and metabolic disorders to children of a similar age who received SCT for acute leukemia in first or second complete remission. This analysis was undertaken to address a reluctance among many physicians to refer children with certain congenital immunodeficiency or metabolic disorders for early SCT. The study population includes 343 children (≤5 years) with congenital immunodeficiency (129 with severe combined immunodeficiency [SCID]; 214 with non-SCID) and 354 children with metabolic disorders. This population was compared to 622 age-matched children with acute leukemia (the control population). All transplantations occurred between 1995 and 2005 and the transplant conditioning regimen was myeloablative. In univariate analysis, 5-year overall survival was higher after HLA-matched sibling donor transplants for SCID (80%), non-SCID (84%) and metabolic disorders (78%) compared to the control group (51%, $p<0.001$). Amongst recipients of unrelated donor SCT, 5-year overall survival was higher for non-SCID patients compared to controls (66% vs 50%, $p = 0.05$). The 5-year survival rates were similar after unrelated donor SCT for SCID (41%), metabolic (51%) and good risk acute leukemia, the control group (50%). In multivariate analysis, donor type was the only factor associated with survival; mortality rates were higher after unrelated donor SCT (odds ratio 1.49, 95% CI 1.02–2.16, $p = 0.04$). Further, we observed no differences in survival after unrelated donor bone marrow and cord blood SCT. The data suggest children with congenital immunodeficiency and metabolic disorders who receive an unrelated donor SCT have similar survival rates as children with good risk acute leukemia. The sub-group of children with non-SCID diseases fare the best, with a 5-year overall survival that exceeds that of age-matched patients with acute leukemia. Therefore prompt referral for SCT for these children, before mounting comorbidities render them ineligible, should be encouraged even in the absence of an HLA-matched sibling donor.

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REDUCED TOXICITY MYELOABLATIVE CONDITIONING REGIMEN WITH BUSULFAN, FLUDARABINE AND ALEMTUZUMAB FOR CHILDREN WITH NON-MALIGNANT DISORDERS, MYELODYSPLASTIC SYNDROME (MDS) AND MYELOID MALIGNANCIES

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Major problems with Busulfan/Cyclophosphamide (Bu/Cy) conditioning are acute toxicities and graft failure. In 2000, we replaced Bu/Cy conditioning with targeted i.v. Busulfan/Fludarabine/rabbit ATG (Bu/Flu/rATG) which effectively reduced acute toxicities; however, graft failure rate remained high (21%). In 2004, we introduced targeted i.v. Busulfan/Fludarabine and Alemtuzumab (Bu/Flu/Campath) to reduce graft failure rate. We describe and compare the outcomes of the first 21 Bu/Flu/Campath study patients (median age 8, range 1–16 years) with those of previously published 19 By/Flu/rATG study patients. Diagnoses included MDS or myeloid malignancy (N = 5), hemoglobinopathy (N = 3), non-SCID primary immunodeficiency (N = 6), aplastic anemia (N = 2), autoimmune disorders (N = 2), and metabolic disorders (N = 3). The donors included ≥8/8 HLA-matched (N = 6) and one antigen mismatched (N = 4) unrelated volunteers, and fully matched related donors (N = 11). Stem cell sources were peripheral blood (N = 9), bone marrow (N = 10) or combined sources (N = 2). 19/20 evaluable patients engrafted. One patient with Hurler's disease developed graft rejection 40 days post transplant but was rescued with a 2nd transplant. The median follow-up of living patients is 21 months (range 4.3–51 months). Estimated 2-year post-transplant overall and event-free survival rates were 83 ± 9% and 71 ± 11%, respectively, which is similar to survival in the Bu/Flu/rATG study (89 ± 7% and 74 ± 10%). Three patients died (at 1, 5, and 12 months post transplant) due to intracranial hemorrhage in 1 patient with Evans syndrome, Aspergillus infection and GVHD in 1 patient with adrenal leukodystrophy (ALD), and disease progression and GVHD in 1 patient with ALD. One patient with MDS relapsed 1 year following the transplant, but is alive following the 2nd successful transplant. CMV reactivated in 47% (7/15) patients who were at risk for reactivation and was successfully treated in all. Only 1 patient developed mild VOD (maximum total bilirubin 3.4 mg/dl). The incidence of acute and chronic GVHD was 15% each, respectively. At last follow up 85% of patients remain mixed chimeras. Bu/Flu/Campath conditioning was well tolerated and resulted in durable mixed chimerism in the majority of patients. Compared with Bu/Flu/rATG, Bu/Flu/Campath conditioning resulted in significantly reduced graft rejection rate (2-tailed Fisher's exact $p = 0.03$) in mismatched MUD transplants, but it did not improve overall survival or event free-survival.

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SECOND ALLOGENEIC STEM CELL TRANSPLANTATION (SCT) IN PEDIATRIC PATIENTS

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Graft rejection and/or disease relapse after allogeneic SCT are ominous events that are often associated with dismal outcome; second SCT may be considered as a salvage alternative in these patients (pts) but is generally regarded as a procedure that is associated with high morbidity and mortality. In the pediatric population, the data on the outcome of second SCT are sketchy and scarce. We present here our experience in 51 pediatric pts who underwent a second SCT at our institution (KFSHRC).

Patients and methods: From May 1996 until May 2008, 51 pts with graft failure or disease relapse after SCT (24 females and 27 males) underwent second SCT at KFSHRC; 17 pts had leukemia, 16 pts had non-malignant hematological disorders (NMHD), 16 pts had immune deficiency disorders (IMD), and 2 pts had metabolic disorders. 35 pts were reconditioned with myeloablative regimens (including 19 pts with TBI-regimens), 7 pts with

serotherapy alone, 6 pts with reduced intensity regimens, and 3 pts received no conditioning. Median age at the second SCT was 6.2 years (range, 0.3–14.2 years) and the median time from the first SCT to the second SCT was 10.3 months (range, 1.2–84 months).

Results: 40 patients had initial engraftment, median time to ANC $\geq 500 \times 10^6$/l was 19 days (range, 9–28 days), and median time to a platelet count $\geq 20 \times 10^9$/l was 26.5 days (range, 10–100 days). Acute grade $\geq$ 3 GVHD, developed in 7 pts (13.7%), mild VOD of the liver developed in 2 pts (3.9%).The 10-year overall (OS) and event free survival (EFS) were 66% and 50% respectively. When survival was evaluated by the interval between the 1st and 2nd SCT: $<$ 6 months (19 pts) and $\geq$ 6 months (32 pts), the 10-year OS was 55% and 73% for the 2 cohorts respectively ($P = 0.05$), and the 10-year EFS was 27% and 67% for the 2 cohorts respectively ($P = 0.005$). With intervals of $<$ 12 months (26 pts) and $\geq$ 12 months (25 pts), the 10-year OS was 64% and 70% for the 2 cohorts respectively ($P = 0.4$), and the 10-year EFS was 42% and 63% for the 2 cohorts respectively ($P = 0.2$). When survival was evaluated by underlying disease, the 10-year OS was 59%, 75% and 59% for pts with NMHD, IMD and leukemia respectively ($P = 0.3$), and the 10-year EFS was 55%, 50%, and 59% ($P = 0.5$) for the same groups respectively.

Conclusions: Second SCT in children is relatively well tolerated and is associated with reasonable survival. OS and EFS appear to be considerably better when the interval between the 2 transplants is $\geq$ 6 months.

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RESULTS OF HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH LEUKOCYTE ADHESION DEFICIENCY TYPE I

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Objective: Hematopoietic stem cell transplantation (HSCT) is the only curative treatment of some congenital immunodeficiency diseases especially leukocyte adhesion deficiency type-I (LAD-I).

Methods: Six patients (3 girls, 3 boys), received allogeneic HSCT between 2007 and 2008. One patient received stem cell from her healthy full human leukocyte antigen (HLA) matched sibling, three patients from their full matched other related (one from father, one from mother and one from uncle which verified with high resolution HLA matching method), one patient from his mother (haploidentical) and one patient from his father with one antigen mismatch. The graft source was bone marrow in 4 patients and peripheral blood stem cells (PBSC) in others. Median age at HSCT was 17 months (10.2–87.8 months). All patients were conditioned with Fludarabine, Melfalan and Antithymocyte globulin (ATG). For graft-versus-host disease (GVHD) prophylaxis, we used Cyclosporine and Methylprednisolone.

Results: All patients engrafted. Median time of Absolute Neutrophil Count $\geq 0.5\times10^9$ /L was +13 and median time of Platelet recovery $\geq 20\times10^9$ /L was +16. Median follow-up of patients was 8 months (range, 1–20 months) and at present five (83%) patients are alive with sustained engraftment and without recurrent infection and improvement of their failure to trive. Three patients developed acute GVHD after transplantation that one of them died because of acute GVHD one month after transplantation. No chronic GVHD occurred. Full chimerism was achieved in one patient and mixed chimerism was achieved in four patients.

Conclusions: Early diagnosis and HSCT of LAD-I rescue patients from lethal disease but not all of patients have full match siblings and others must transplanted from other related, haploidentical relative, non relative full match or cord blood. Analysis of our patients who developed mixed chimerism suggested that this mixed chimeric state resulted in a reversal of the LAD-I phenotype.

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STABLE MIXED CHIMERISM AFTER NON-MYELOABLATIVE TRANSPLANT FOR SICKLE CELL DISEASE: NORMAL HEMATOPOIESIS DOMINATES OVER ABNORMAL IN MIXED CHIMERISM

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Allosensitization due to transfusion therapy has been a barrier to engraftment in patients with sickle cell (SC) disease, requiring the use of more intense conditioning. In a mouse model, sensitization to bone marrow cells (BMC) results predominantly from the humoral immune response. We added alemtuzumab (anti-CD52) lymphodepletion for conditioning recipients for a hematopoietic cell transplant. 2 cycles of alemtuzumab were administered with the rationale of eliminating memory B cells by inducing them to undergo homeostatic proliferation after the 1st round of depletion. Conditioning consisted of alemtuzumab (10 mg/day, days -53— -50 and days -24 —-21), fludarabine (30 mg/m^2/day days -5 —-3), 200 cGy TBI (day -1), matched related donor BM infusion day 0, followed by cyclosporine and mycophenolate mofetil (day-1—$>$10 months). 2 patients have been transplanted. Patient 1 was 7 at transplant, with a history of multiple pain crises, episodes of acute chest syndrome, and extensively treated with exchange transfusion therapy and hydroxyurea. She received 14.5×10^6kg CD34 cells from her HLA-identical sibling donor with SC trait, showing 78% donor engraftment day 30. Her RBC production remained phenotypically trait which is compatible with donor hematopoiesis $>$ 615 days post-transplant, with donor lymphoid and myeloid chimerism consistently 20–30%. Immunosuppression was discontinued 10 months post-stem cell transplantation (SCT). Patient 2 was 9 at transplant with multiple pain crises, 2 episodes of acute chest syndrome before transplant, and had been treated with exchange transfusions for 7 years. He received HLA-matched sibling donor BM, processed to deplete T- and B cells. The graft contained 5.24×10^6/kg CD34, 0.55×10^6/kg $\alpha\beta$-TCR and 0.35×10^6/kg FC cells. He has been transfusion-independent post-SCT, with 100% donor RBC production and chimerism levels at 20–30% donor by FISH $>$851 days post-transplant. Immunosuppression was discontinued at 23 months post-SCT. Neither patient had GVHD, transplant-related toxicity, or SC complications since transplant. Data suggest that the addition of an alemtuzumab split-course to a nonmyeloablative transplant regimen allows hematopoietic cell engraftment of allosensitized recipients with SCD without GVHD. Stable mixed chimerism of myeloid and lymphoid lineages is accompanied by full donor erythropoiesis. Stable mixed chimerism may also have been achieved due to prolonged post-SCT immunosuppression from MMF.

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BONE MINERAL DENSITY, LEAN BODY MASS, CALCIUM AND VITAMIN D INTAKE IN CHILDREN AND ADOLESCENTS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: Hematopoietic stem cell transplantation (HSCT) has been associated with decreased food intake, malnutrition, reduced lean body mass and reduced bone mineral density (BMD), which might result in increased morbidity and mortality. The purpose of this study was to evaluate the BMD, lean body mass, calcium and vitamin D intake in children and adolescents before and 6 months after HCT.

Patients and Methods: Forty patients (25 boys and 15 girls; mean age: 10,1 $\pm$ 4,2 $\pm$ yrs) who were consecutively submitted to allogenic HSCT between September 2006 and March 2008 and survived after 6 months were included in the analysis. BMD was evaluated by DXA (HOLOGIC-1000) at the lumbar spine (LS) and whole body (WB), lean body mass by bioelectrical impedance analysis and food intake by a 24 hours recall and food frequency questionnaire.

Results: LS BMD was 0,673 $\pm$ 0,167 g/cm^2 in the first evaluation and 0,662 $\pm$ 0,78 g/cm^2 in the second evaluation ($p > 0.05$). The WB BMD was 0,850 $\pm$ 0,164g/cm^2 in the first evaluation, reducing to